REMARKS

Entry of the foregoing and reexamination and reconsideration of the subject application, as amended, pursuant to and consistent with 37 C.F.R. § 1.112, are respectfully requested in light of the remarks which follow.

The Office Action Summary states that claims 1-3, 5-8, 13-18, 21-23, 27-28, and 33-46 are pending, and that claims 5-8, 21-23, 27-28, and 33-46 stand withdrawn. Applicants note that claims 4-6, 9-12, 24-26, 29-32, and 47-54 were canceled in Applicants' Amendment dated January 19, 2005. Thus, Applicants consider the following claims as pending: 1-3, 7-8, 13-18, 21-23, 27-28, and 33-46, as set forth by the Office at the top of page 2 of the Detailed Action.

Claims 7-8, 21-23, 27-28 and 33-46 are canceled herein without prejudice or disclaimer thereto. Applicants reserve the right to file at least one continuation application directed to any subject matter canceled herein.

Claims 1, 13, and 14 are amended herein. Basis for the amendments may be found throughout the specification and claims as-filed, especially at paragraphs 0007, 0013, and 0017. Thus, no prohibited new matter is presented by way of the present Amendment.

Applicants note the acknowledgement by the Office of the election of Group I.

Claim Rejections Under 35 U.S.C. § 112, first paragraph-- Enablement

Claims 1-3, 13-16 and 18 stand rejected under 35 U.S.C. §112, first paragraph for allegedly being non-enabled. The Office states claims 1-3, 13-16 and 18 are rejected because the specification, while enabling for a method of contacting hippocampal neurons under *in vitro* conditions with an amount of isolated nucleic

acid encoding full-length TrkB, does not reasonably provide enablement for a method of contacting hippocampal neurons under *in vivo* conditions with an amount of isolated nucleic acid encoding full-length TrkB or any mutal, variant, homolog, or fragment thereof having the same activity as said full-length TrkB. Applicants traverse.

Applicants respectfully note that, as a matter of law, the disclosure of *in vitro* use for TrkB, combined with the Examiner's admission that the present claims enable the use of TrkB *in vitro*, is sufficient to enable the present claims, as amended herewith. A rigorous or an invariable exact correlation between *in vitro* and *in vivo* is not required, as stated in *Cross v. Iizuka*, 7553 F.2d 1040, 1050, 224 USPQ 739, 747 (Fed. Cir. 1985), or *In re Brana*, 51 F.3d 1560, 1566, 34 USPQ2d 1436, 1441 (Fed. Circ. 1995) (*see* M.P.E.P. §2164.02). *In re Brana*, the Court stated, "A specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented *must* be taken as in compliance with the enabling requirement of the first paragraph of § 112 *unless* there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support."

Further, M.P.E.P. § 2164.02 states, "If the art is such that a particular model is recognized as correlating to a specific condition, than it should be accepted as correlating unless the Examiner has evidence that the model does not correlate." Applicants respectfully refer the Examiner to paragraphs 0005 and 00122 of the present specification in which Applicants describe using Ts16, a well-known mouse model for Downs Syndrome. Applicants respectfully assert that the use of this well-

known *in vivo* mouse model (Ts16) correlates to a specific neuro-developmental condition, and provides sufficient enablement for the scope of Applicant's claimed invention.

In addition, Applicants have amended the claims herein to recite a method of treating a neurodegenerative disorder or a neuro-developmental disorder comprising the step of contacting neuropathic hippocampal neuron with an amount of a vector sufficient to alter the ratio of amount of full-length TrkB polypeptide to truncated TrkB polypeptide in said neuron.

In view of these comments and amendments to the claims, Applicants respectfully assert that the rejected claims are enabled under 35 U.S.C. § 112, First Paragraph. Therefore, Applicants respectfully request reconsideration and withdrawal of this rejection.

Claim Rejections Under 35 U.S.C. § 112, first paragraph--Written Description

Claims 1-3, 13-16 and 18 stand rejected under 35 U.S.C. § 112, first paragraph, for allegedly lacking written description. The Office notes "case law supports a finding that the claim has written description for a nucleic acid encoding TrkB, but not variants, homologs, or fragments thereof of TrkB having the same activity as full-length TrkB. Therefore, the Office argues that only the TIMP3 gene encompassed by SEQ ID NO:1, but not the full breadth of the claims meet the written description provision of 35 U.S.C. § 112, first paragraph." (Office Action, page 9).

Applicants respectfully request clarification regarding the Office's reference to "... the TIMP3 gene encompassed by SEQ ID NO:1". A review of the entire

specification reveals no reference is ever made by the Applicants to a TIMP3 gene. Applicants assume the Examiner intended to refer to the "TrkB" gene and not to a "TIMP3" gene. Applicants' response herein is based on this assumption.

Applicants respectfully note that claims 1-3, 14-16 and 18 are amended herewith to reference full-length TrkB. Further, Applicants note that description for the nucleotide and amino acid sequences of both the human full-length TrkB and the human truncated TrkB isoforms is provided in paragraphs 0042-0053 of the specification as-filed.

In view of these comments and amendments, Applicants respectfully assert that the rejected claims are sufficiently described to meet 35 U.S.C. § 112, first paragraph. Therefore, Applicants respectfully request reconsideration and withdrawal of this rejection.

Claim Rejections Under 35 U.S.C. § 112, second paragraph

Claims 1-3, 13-16 and 18 stand rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite. The Office states that the rejected claims are unclear with regard to any mutant, variant, homolog, or fragment thereof having the same activity as full-length TrkB.

In response, without acquesing in the rejection, Applicants have amended the claims herewith to recite a "method of treating a neuro-degenerative disorder or a neuro-developmental disorder comprising the step of contacting a neuropathic hippocampal neuron with an amount of a vector sufficient to alter the ratio of amount of full-length TrkB polypeptide to truncated TrkB polypeptide in said neuron." Thus, this rejection is obviated.

Claim Rejections Under 35 U.S.C. § 102(b)

Claims 1-3, 13-16 and 18 stand rejected for allegedly being anticipated under 35 U.S.C. § 102(b) in light of Kryl et al. (1999).

The Office states that Kryl et al. teach hippocampal neurons transfected with cDNA comprising either full-length TrkB or the truncated T1 form of TrkB, and that the transfected hippocampal neurons showed even distribution of full-length and truncated TrkB in all areas of the cell culture (*see* paragraph 23 of the Office Action).

In order for anticipation to occur under 35 U.S.C. § 102, the reference must teach every aspect of the claimed invention. Any feature not directly taught must be inherently present in the reference (*see* M.P.E.P. § 706.02). Kryl et al. disclose the use of adenoviruses to introduce epitope-tagged full length and truncated TrkB into a variety of cells including primary cultured rodent neurons. However, the instant claims are drawn to a method of introducing full-length TrkB into vulnerable neurons to treat neuro-degenerative disorder and/or a neuro-developmental disorder. Applicants discovered unexpectedly that vulnerable neurons expressing increased TrkB receptor mitigate premature neuron death that characterizes neurodegenerative and/or neuro-developmental disorders (*see* for example, paragraphs 00122-00129 of the specification).

In addition, Kryl et al does not disclose that increasing the expression levels of TrkB receptor is a prerequisite for therapeutic efficacy. Instead, Kryl et al. introduce unknown amounts of exogenous Trk proteins tagged with fluorescent probes in order to determine the spatial distribution of the Trk receptors within the cells. The neurons of Kryl et al. are not vulnerable (*i.e.*, neuropathic). Further, Kryl et al. do not

teach or reference in any way the therapeutic benefit of increasing TrkB in a neuropathic neuron. Accordingly, Kryl et al. do not teach Applicants' invention.

In view of these comments and amendments made to the claims, Applicants respectfully assert that none of the rejected claims are anticipated in view of Kryl et al. Therefore, Applicants respectfully request reconsideration and withdrawal of this rejection.

CONCLUSION

From the foregoing, further and favorable action in the form of a Notice of Allowance is respectfully requested and such action is earnestly solicited.

In the event that there are any questions concerning this amendment or the application in general, the Examiner is respectfully requested to telephone the undersigned so that prosecution of the application may be expedited.

Respectfully submitted,

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